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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,119	01/12/2001	Sarah S. Bacus	MBHB01-034	1978

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
09/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/760,119	BACUS, SARAH S.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9,11,12 and 14-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4-9,11,12 and 14-16* is/are allowed.

6)☒ Claim(s) *17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 12 and 15 have been amended. Claims 17-19 have been added. Claims 1, 2, 4-9, 11, 12, 14-19 are pending and under consideration.

After review and reconsideration, claims 1, 2, 4-9, 11, 12 and 14-16, limited to the detection of SA Beta-Gal and p21 are given priority to 60/176,515 and 60/176,514, both filed January 12, 2000. Claims 17-19, incorporating markers in the instant method not described in the provisional documents, will have an effective priority date of January 12, 2001..

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roninson et al (U.S. 2004/0058320, priority to 60/257,907 filed December 21, 2000, cited in a previous Office action).

Roninson et al teach a method comprising a method for monitoring the efficacy of treatment by detecting senescence associated markers in biopsy samples obtained after patient treatment (paragraph [0023] and paragraph [0048]). Roninson et al teach (a)obtaining a biological sample comprising tumor cells from an animal before and after treatment; (b) comparing expression of at least one gene in Table I, 2A or 2B after treatment with expression of said gene or genes before treatment and(c) determining that said treatment has efficacy for treating the tumor if expression of at least one gene in 2A or 2B is higher after treatment, and expression of at least one gene in Table 1 is lower after treatment than before treatment (claims 86 and 87). Roninson et al teach that p21 is up regulated (Table 2B) in doxorubicin treated HCT116 cells which are colon carcinoma cells (paragraph [0055]). Roninson et al teach that doxorubicin as a chemotherapeutic agent which can induce senescence in clinical samples

(paragraphs [0004], [0007], [0042, second column, line 8] and [0059]. Roninson et al teach that staining for SA-beta-Gal is indicative of a senescent phenotype (paragraph[0057]) and that HCT116 cells can be separated into two different populations after doxorubicin treatment: a senescent cell population and a population that regained the capacity to proliferate (paragraph[0058]). Roninson et al teach a preferred embodiment wherein the gene in Table 2A is BTG1, BTG2, EPLIN, WIPI, Maspin, MIC-1, IGFBP-6 or amphiregulin (paragraph [0019]). Roninson et al teach that multiple growth-inhibitor genes were induced by doxorubicin treatment to result in the maintenance of doxorubicin-induced cell cycle arrest in the absence of p16 which is not expressed in HCT116 cells (paragraph [0065]). Roninson et al teach that EPLIN is strongly up regulated in breast carcinoma cells after treatment with agents known to produce senescence-like growth arrest (paragraphs [0042] and [0089]). Roninson et al further teach that Maspin is down regulated in advanced breast cancer (paragraph [0066]) consistent with the hypothesis that drug-induced growth arrest to tumor cells is maintained by a set of apparently redundant intracellular and paracrine factors (paragraph [0066]).

It would have been prima facie obvious at the time that the claimed invention was made to monitor senescence in breast tumor cells taken from a patient before and after administration of doxorubicin by staining for SA-Beta-Gal. One of skill in the art would have been motivated to do so by the general teachings of Roninson et al on monitoring the efficacy of treatment by detecting senescence associated markers in biopsy samples obtained after patient treatment; and the specific teachings regarding staining for SA-Beta Gal as indicative of a senescent associated phenotype; and the up-regulation of EPLIN in doxorubicin treated MCF7 breast carcinoma cells. One of skill in the art would have been motivated to monitor senescence induced by doxorubicin in patients having breast tumors because Roninson et al teach that doxorubicin-treated HCT116 cells can be separated into two populations, one being permanently senescent and the other having the capacity to regain the ability to proliferate.

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roninson et al (U.S. 2004/0058320, priority to 60/257,907 filed December 21, 2000) in view of Bacus (U.S. 4,741,043, cited in a previous Office action).

Claim 18 embodies the method of claim 17 wherein SA-B-Gal activity, p27 expression, p16 expression, or a combination thereof is detected. Claim 19 embodies the method of claim 18 wherein the detecting comprises staining the first and second tissue or cell sample for SA-Beta-Gal activity, p27, p16, or any combination thereof, and measuring the optical density of one or more stained cells.

Roninson et al teach that expression of the corresponding genes in Table 2 can be measured at the protein level, using antibodies against the corresponding gene products for in situ immunostaining (paragraph [0048]), which meets the limitation of "stained cells" in claim 15. Roninson et al do not specifically teach determining the "optical density" or one or more stained cells.

Bacus teaches the determination of optical density by image analysis (column 2, lines 28-29). Bacus teaches that image analysis overcomes staining differences due to ah to batch variations in stains (column 2, lines 16-42). Bacus teaches that image analysis is applicable to the analysis of cells as "objects" and in particular to the binding of a monoclonal antibody conjugated to a stain (column 3, lines 42-57).

It would have been prima facie obvious at the time that the claimed invention was made to analyze the optical density resulting from the in situ immunostaining of biopsy samples of Roninson et al by image analysis. One of skill in the art would have been motivated to do so by the teachings of Bacus on the advantages of image analysis for analyzing cells bound by a monoclonal antibody conjugated to a stain..

All other rejections and objections as set forth or maintained in the previous Office action are withdrawn.

Claims 1, 2, 4-9, 11, 12 and 14-16 are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643